

Br. 874 368

PATENT SPECIFICATION

NO DRAWINGS

874.368



Date of Application and filing Complete Specification: Sep. 16, 1958.

No. 29608/58.

Application made in United States of America on Dec. 9, 1957.

Complete Specification Published: Aug. 2, 1961.

Index at acceptance:—Class 81(1), B1(B2: C: G: R1: R2: S: Z), L4.

International Classification:—A61k.

COMPLETE SPECIFICATION

Improvements in Anti-Seborrheic and Scalp Preparations

I, IRWIN IRVILLE LUBOWE, a citizen of the United States of America, of 667, Madison Avenue, New York 21, New York, United States of America, do hereby declare the invention, for which I pray that a patent may be granted to me, and the method by which it is to be performed, to be particularly described in and by the following statement:—

The present invention relates to the provision of an improved anti-seborrheic and scalp preparation containing hormones and amino acids.

A preparation according to this invention forms an emulsion particularly suitable for the treatment of seborrhea or seborrhea capitis in that the preparation restores the normal physiological function of the sebaceous glands.

The improved preparation for the treatment of the hair and scalp comprises a stable emulsion containing:—

- (a) an estrogenic hormone as herein defined
- (b) a progestational hormone as herein defined
- (c) the sulphur bearing amino acid methionine or its simple compounds or derivatives e.g. acetylmethionine and allantoin acetyl methioninate
- (d) an α -amino acid

the said preparation having a pH value between 6.0 and 8.6.

I have found that there is a synergistic action which is obtained with the improved preparation which is not obtained by any of the essential ingredients of the preparation when used singly.

The preferred preparation contains estrogenic hormones in quantities between 25,000 to 50,000 International Units per kilogram of the preparation, glycine being added to an amount between 0.1% and 10% by weight of the total weight of the preparation, and progestational hormones in quantities between 25 to 100 milligrams per kilogram of the preparation.

With the use of this preparation, it has been found that the dandruff or flaking of the scalp

[Price 3s. 6d.]

has been relieved and eliminated. The itching disappears after several applications. The texture of the hair is thickened and becomes strengthened and less subject to brittleness and subsequent breakage.

Folliculitis or infection of the sebaceous glands or hair follicles disappears after several days topical application of the above formulation.

The appearance of the epidermis of the scalp is improved, particularly because of the improved local circulation which favourably affects the cutaneous tissue and the pilosebaceous appendage.

Furthermore, it has been noted after many trials that treatment with this preparation counteracts irritation and sensitivity often accompanying permanent waving, bleaching and dyeing of the hair.

It has been observed that treatment with the above preparation for three to four days, at least twice a day, will prevent many resultant irritations and erythema which follows permanent hair waving, bleaching and dyeing applications of the hair.

Methionine, which is a methylated, sulphur-containing, amino acid, has been found to be surprisingly effective in the above composition.

My experiments show that methionine is unexpectedly absorbed by the hair and hair follicles, and synthesizes itself into protein complexes or forms part of the protein complexes found in both the scalp and scalp appendages.

It has been found that a stable mixture of progestational hormones and estrogenic hormones is most effective in catalyzing absorption of the methionine into the scalp and scalp appendages.

Simple compounds and derivatives of methionine such as acetyl methionine and allantoin acetyl methionine may replace the methionine in the composition of the invention in which case the preparation may be applied in the form of a topical solution to the hair and scalp, because of increased solubility.

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The improved preparation is most effective when it includes estrogenic hormones, methionine, glutathione, cystine and progestational hormones. It appears that the estrogenic hormones surprisingly exert a hyperplastic action upon the cellular structure of cutaneous tissue.

Progestational hormones and estrogenic hormone overcome the adverse effect of the excessive secretion of testosterone, the androgenic hormone upon the sebaceous activity.

Methionine, glutathione and cystine when employed together with an estrogenic hormone and a progestational hormone are effective both in preventing or minimising inflammatory or diseased conditions favouring the shedding of hair, and also in promoting normal physiological function of the pilo-sebaceous apparatus.

Particularly it has been found that a preparation containing methionine, glutathione, cystine and estrogenic and progestational hormones in ethyl alcohol and pyrrolidone compounds such as 2-pyrrolidone will be rapidly absorbed, to regulate and promote normal keratinization of the pilo-sebaceous glands and epidermal cells.

The methionine, glutathione and cystine may be added in a total proportion of 0.1% to 20% by weight and preferably in the range 0.1% to 10% by weight of the finished preparation. Preferably the amount by weight of progesterone used is 5 to 15 parts.

The most suitable vehicle for these active constituents consists of water and ethyl or isopropyl alcohol, and may also include other constituents such as conventional wetting, dispersing and emulsifying agents such as polyvinyl, pyrrolidone and salts of higher aliphatic alcohols, higher aliphatic alcohols and their esters ointments bases, perfumes and dyes.

Any additional materials considered desirable for their emollient or other physiological action or effect may also be incorporated. It will be understood that the estrogenic hormones for use in the preparation according to the invention may be a natural product or an equivalent synthetic substitute.

Trace minerals such as copper, zinc, magnesium or manganese can also be included. Cepharanthine and its salts, after my clinical evaluation, were found to exert a beneficial action in stimulation of the pilo-sebaceous apparatus. These alkaloidal chemicals possess antispasmodic and vasodilating properties — particularly of the cutaneous tissues. The above minerals and alkaloids act synergistically together with estrogenic and progesterone hormones and form an effective therapeutic anti-seborrhoeic and scalp preparation.

Antibiotics have been found effective when added to the preparation.

Estrogenic hormones that can be employed are estrone, estradiol, stilbesterol and dienestrol.

The following are examples of some preparations according to the invention which may be utilised and which may have a pH value of 6.0 to 8.5.

The introduction into the preparation of bacteriocidal, fungicidal, and pityrosporum ovalicidal compounds have a favourable effect in the reduction of itching, scaling, seborrhea, folliculitis and crusting of the scalp.

The preferred bactericidal compounds are 2:4 dichlorophenyl benzene sulfonate (Genite), quaternary ammonium salts such as benzalkonium chloride, halogenated phenols and organic sulfates. Additional antiseptic compounds are hexachlorophene, bithionol and thiuram.

EXAMPLE I

	Specific	Range
Progesterone	15 Mg.	5 to 25 Mg.
Estrogenic hormone	1 Mg.	1 to 3 Mg.
Methionine	2 g.	1 to 5 g.
Glycine	2 g.	1 to 5 g.
2:4 dichlorophenyl benzene sulfonate	1 g.	$\frac{1}{2}$ to 5 g.
Methyl or ethyl diamino ethyl glycine hydrochloride	1 g.	$\frac{1}{2}$ to 5 g.
2 - Pyrrolidone	2 g.	5 to 15 g.
Ethyl alcohol	to make 100 grams	

EXAMPLE II

Estrogenic hormone	2 to 10 Mg.
Progesterone	10 to 50 Mg.
Methionine	1 to 5 g.
Glycine	1 g.
Gluthathione	5 mg.
2 - Pyrrolidone	2 to 5 g.
Ethyl Alcohol	90 g.

EXAMPLE III

Estrogenic hormone	5 Mg.
Progesterone	10 to 50 Mg.
Zinc phenol sulfonate	3 to 5 g.
Acetyl Methionine	1 to 5 g.
Polyvinylpyrrolidone	2½ g.
2 - Pyrrolidone	12½ g.
Alkyl diamino ethyl glycine hydrochloride	2 to 5 g.
2:4 Dichlorophenyl benzene sulfonate	5.0
Ethyl alcohol	65.0

EXAMPLE IV

Estrogenic hormone	100,000 I.U.
Progesterone	25 Mg.
Methionine	0.15 g.
Cystine	2.50 g.
Glutathione	2.50 g.
Gelatin	2.50 g.
Polyethylene glycol (average mol. wt. 300)	150.00 ml.
Industrial methylated spirits (toilet preparations grade)	300.00 ml.
Physiological saline solution, q.s. to make	1000.00 ml.

EXAMPLE V

Progesterone	15 Mg.
Natural Estrogenic hormone	5 Mg.
Methionine	3 g.
Glutathione	3 g.
Tyrosine	50 Mg.
Benzyl alcohol	30 millilitres
Propylene glycol	150 millilitres
Fatty acid esters of polyethylene glycol molecular weight 400	50 millilitres
Water, to make	1000 millilitres

EXAMPLE VI

Natural estrogenic hormone	5 Mg.
Progesterone	15 Mg.
Cystine	1.0 g.
Phenyl alanine	0.5 g.
Glutathione	.01 g.
Methionine	2 g.
Isopropyl myristate	30.0 millilitres
Diethylene glycol monoethyl ether	60.0 g.
Mixed palm kernel fatty acid esters of polyethylene glycol molecular weight 400	20.0 milliliters
Benzyl alcohol	55.0 millilitres
Terpineol	15.0 millilitres
Polyethylene glycol molecular weight 200	30.0 millilitres
Distilled water	140.0 millilitres
Industrial methylated spirits (Toilet preparations grade)	650.0 millilitres

EXAMPLE VII

Estrogens	10 Mg.
Progesterone	50 Mg.
Cystine	50 Mg.
Tyrosine	50 Mg.
Gelatin	2 g.
Methionine	2 g.
Glycine	2 g.
Cera (Registered Trade Mark) emulsificans (a combination of stearyl and cetyl alcohols)	20 g.
Triethanol amine lauryl sulphate	5 g.
Vegetable oil, such as sesame oil or sweet almond oil (cosmetic grade)	70 millilitres
Isopropyl myristate	40 millilitres
Propylene glycol	60 millilitres
Water, to make	1000 millilitres

5 A vasodilator such as butyl or methyl or ethyl or furfuryl nicotinate in amounts of from $\frac{1}{2}$ to 2% by weight of the total preparation may be included in the composition of the invention. The pH is regulated to vary between 6.0 to 8.5, and 1 to 4% of lanolin solubilized with isopropyl palmitate or myristate may be added if desired. Other substances for example 10 1 to 4% of gelatin and 1 to 4% of the mono-oleate, the monolaurate, or the monopalmitate of polyethylene glycol or glycerol may also be added. All of these percentages are by weight. It is desirable to use 1 to 3% of an amino acid 15 such as, for example, an alkyl diamino-ethyl glycine hydrochloride as a penetrating agent.

In cases where a preparation according to the invention has been employed for seborrhea capitis, there has been noted an improvement 20 of the texture of the skin of the scalp area, with rapid decrease and elimination of crusting and scales, and with subsequent relief of itching.

Patch testing with the above formulations upon 200 human subjects according to the methods described by the United States Food and Drug Administration reveals no evidence of primary irritation or cutaneous sensitization. 25

Histological examination of patients treated 30 with this composition reveals increased vasodilation of the subcutaneous areas, and cellular

infiltrate of the sebaceous follicular areas, indicating transcutaneous penetration to the follicular area.

Examination of the conjunctiva of animals following instillation of a preparation according to this invention reveals no irritation of the cornea. The routine Draize test prescribed by the United States Food and Drug Administration was followed. 35 40

Bacteriological tests indicate that with the inclusion of 2:4 dichlorophenyl benzene sulfonate, the preparation according to this invention inhibits the growth of pityosporum ovale, a fungus which has been considered as one of the causative organisms in the production of seborrhea capitis. 45

The above sulfonate has also been found to be bacteriocidal against staphylococcus albus and aureus, which are bacterial organisms which cause pyogenic infections of the skin in association with seborrhea capitis. 50

The above sulfonate has also been demonstrated to be fungicidal against microsporum lanosum which is a causative agent in producing tinea capitis; known as ringworm of the scalp. 55

Clinical evaluation conducted upon over 300 patients reveals the effectiveness and the non-toxicity of the preparation according to the invention which is effective in rapidly clearing 60

the scalp of itching, scaling, and infections of the pilo-sebaceous apparatus, which are symptoms of seborrhea capitis.

5 The "estrogenic hormones" for use in the preparation according to the invention may be natural or synthetic hormones and may be water soluble or water insoluble. Estrogenic hormones include estrone, estradiol, stilbesterol, dienestiol or any other hormone having estrogenic action by which I mean producing estrus
10 which is a cyclic change in the female genital tract and also having secondary effects of a sexual nature concerning the skin, hair and mammary glands.

15 The term "progestational hormone" means progesterone or one of the many new synthetic compounds which have progestational action. By progestational action I mean that the hormone is capable of initiating and maintaining the secretory phase of endometrium of the
20 uterus so that a synthetic or natural hormone having progestational action when taken internally or injected will produce a premenstrual phase. However, the effects produced when a progestational hormone is applied topically to
25 the skin and hair are not considered to be side effects but are unexpected and unusual effects in that the pilosebaceous members, that is the hair and sebaceous glands are stimulated and their function heightened and accelerated.
30

WHAT I CLAIM IS:—

1. A preparation for the treatment of the hair and scalp comprising a stable emulsion containing:—

- 35 (a) an estrogenic hormone as herein defined
(b) a progestational hormone as herein defined

(c) the sulphur bearing amino acid methionine or its simple compounds or derivatives e.g. acetyl methionine and allantoin acetyl methioninate. 40

(d) an α -amino acid
the said preparation having a pH value between 6 and 8.6

2. A preparation according to claim 1 45 wherein the α -amino acid is present in the preparation in an amount between 0.1% and 10% by weight of the total weight.

3. A preparation according to claim 1 or 2 wherein the α -amino acid is glycine. 50

4. A preparation for the treatment of the hair and scalp comprising a stable emulsion of estrogenic hormones, progesterone, glutathionine, methionine and an α amino acid, the said preparation having a pH value between 6.0 and 8.6 and the α amino acid being present
55 in the preparation in an amount between 0.1% and 10% by weight of the total weight.

5. A preparation according to any of the preceding claims wherein the estrogenic hormone is used in a proportion of 25,000 to 500,000 International Units per kilogram of the finished preparation. 60

6. A preparation according to claim 1 or 4 wherein the progestational hormone is included in a proportion of 25 milligrams to 100 milligrams per kilogram of the finished preparation. 65

7. A preparation for the treatment of the hair and scalp substantially as hereinbefore described. 70

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